U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE

NATIONAL INSTITUTES OF HEALTH
NATIONAL INSTITUTE OF BIOMEDICAL IMAGING AND BIOENGINEERING
(NIBIB)

GUIDELINES FOR PREPARING NIBIB P41 BIOMEDICAL TECHNOLOGY
RESOURCE CENTER APPLICATIONS

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A. GENERAL DESCRIPTION

Biomedical Technology Resource Center (P41) grants support novel, cutting-edge, multi-disciplinary technology development programs that are targeted towards a wide range of biomedical applications. Each P41 Center is focused on a particular experimental or computational technology, or a suite of technologies in a topic area, and serves the needs of a large, broadly-based community of users. It is expected that the needs (and composition) of this community of users will change significantly over time, and that the technology development component of the Center will be continually modified to respond rapidly and effectively to emerging biomedical research opportunities. Centers are funded for up to five years, and may apply for competing renewals.

P41 Centers contain five components: technological research and development (R&D Core projects), collaborative research projects, service, dissemination and training. Each of these components will be discussed in more detail below.

1. Technological Research and Development (Core) Projects

Technological R&D Core projects should be at the cutting edge of the specific research and development area, and should respond rapidly to the emerging needs of the biomedical research community, with the goal of increasing the usefulness of the technology in biomedical research. A minimum of three technological R&D projects constitute the Core section of the P41 Center grant. Since it is expected that these projects will involve multidisciplinary science and engineering, the Core projects may or may not be physically located at a single site. If more than one site is involved, solid evidence of strong communication and collaboration among projects at distant sites should be provided.

Technological R&D projects may involve the development and application of new biomedical imaging and/or bioengineering technologies, or the significant improvement of existing technologies, to advance basic research and/or medical care. It is anticipated that projects may involve the integration of the physical, engineering, and computer sciences with the life sciences. Only scientific and technological proposals that are directly relevant to the NIBIB mission (http://www.nibib.nih.gov/About/MissionHistory#Mission) will be considered. Current areas of high programmatic interest are listed on the NIBIB website at http://www.nibib.nih.gov/Funding/Strategies/NIBIBPrograms/BRPGuides.

2. Collaborative Research Projects

In collaboration with investigators from other regional and national academic and industrial institutions, P41 Center staff should continuously develop significant new applications of the Resource technology in the biomedical sciences. This is best accomplished through high-quality collaborative research projects that are closely related to core technology R&D. These collaborative projects involve experts in the technology, usually Resource Center personnel, working jointly with investigators outside the resource who have expertise in a particular biomedical discipline. Such efforts should lead to joint publications and, in some cases, patents, licenses or various levels of FDA approvals. The collaborations should drive the technological

R&D, and the technology should significantly advance the scientific frontiers of the collaborative research projects.

3. Service

The P41 Center must provide biomedical researchers, on a national level, with access to the technology developed in the Center. This includes making available specialized instrumentation, equipment, software and techniques, and offering consultation and technical assistance in their use. Service is characterized by a routine operation of resource equipment or methods in which P41 Center personnel have little intellectual role, and generally do not share in authorship on resulting papers or patents. However, the P41 Center should be acknowledged in papers resulting from service projects. While service is one of the key elements of the Resource, the P41 mechanism is not intended to support centers that are predominantly service-oriented.

4. Training

The P41 Center must provide regular training to collaborators and service users, on a national level, on the technologies available in the Center. Training must be provided through hands-on laboratory experience, seminars, and lectures. Short courses, symposia, and workshops on appropriate topics that bring together researchers, often from multidisciplinary areas, are important in introducing the national research community to potential applications of the P41 Center technology in biomedical research. Training can be offered periodically, often in conjunction with meetings that the user community is likely to attend.

5. Dissemination

The P41 Center must inform the scientific community about the technology available in the Center, and the accomplishments of the Center, by publishing articles, books, patents, newsletters, annual reports, special issues of technical journals, press releases, presenting research results at meetings, conducting conferences, distributing software products, or transferring technologies to industry where they will be distributed widely. In resources that are developing software, emphasis should be placed on producing portable, well-documented, user-friendly software, and making it readily available to the user community. The P41 Center is expected to maintain an up-to-date website.

6. Scientific Advisory Board

The Scientific Advisory Board (SAB) is appointed by the principal investigator (PI) and assesses the progress made by the Center as well as provides advice on future directions for the Center, priority setting, and allocation of Center resources. The board chair should be knowledgeable in the Center technology and the science it serves, but should not be a member of the Center staff, or a major user of the Center. The remaining board membership should be balanced among scientists knowledgeable in the Center technology, experts in the application of the technology to biomedical research problems, and users of the technology. Board members should be from the geographical regions served by the Center, and membership should be rotated periodically.

The board chair and a majority of members should be from outside the host institution. The SAB should meet at least annually at the P41 Center and prepare a written report of its recommendations. This report, and an action plan from the PI in response to the

recommendations, must be included as part of the Center's Annual Progress Report. The SAB should meet approximately one to two months prior to submission of the Annual Progress Report.

B. CRITERIA FOR CONSIDERATION FOR A P41 RESOURCE CENTER GRANT

P41 Centers must be focused on technology development. The technology being developed may center on a single technology, instrument or software, or may be focused around themes or suites of tools to build systems-like expertise in a particular topic area. P41 Centers coordinate and conduct five different activities: 1) technological R&D; 2) collaborative research; 3) service; 4) training; and 5) dissemination. The technological capabilities of the P41 Center must be state-of-the-art and not broadly available by other means. The projects served by the new technology must be broad in scope and involve a variety of biomedical research areas. The resource is expected to serve investigators in a wide geographical region; preferably across the nation.

C. FUNDING PLAN FOR A P41 RESOURCE CENTER GRANT

The P41 Center Program provides support for the establishment and initial user operations of a Center. It is not a requirement that every element of the Center infrastructure be present at the time of submission of the P41 application; however, plans for how the infrastructure will quickly be put into place are needed. Continued support depends primarily upon the merit of the technology R&D and its application to important biomedical problems. P41 Centers are not intended to serve selected users or laboratories on a permanent basis. Long-term collaborative and service users are expected to acquire separate funding for their technology needs either directly, or through shared support of the Center. Costs of routine service activities should also be shared, for example, through joint grant support, institutional funding, or a charge back system. For details on how to report program income obtained through a charge back system see instruction under "Service" on page 8.

D. TYPES OF P41 RESOURCE CENTER GRANTS CURRENTLY SUPPORTED

The NIBIB P41 Center program is responsible for supporting the development of cutting-edge technologies that could potentially have a major impact on basic biomedical research and medical care. A directory of currently funded NIBIB P41 Biomedical Technology Resource Centers is available on the NIBIB website at: http://www.nibib1.nih.gov/Research/ResourceCenters. The absence of a particular technology from this list does not necessarily mean that the NIBIB would not consider a P41 application in that area. In addition, Centers do not need to be focused on a particular instrument or piece of software. A broader suite of tools to build systems-like expertise in a topic area is acceptable. Potential applicants are encouraged to contact NIBIB program staff for further information.

E. INSTRUCTIONS FOR APPLICANTS

1. Eligibility

P41 Center Grants are limited to Principal Investigators at institutions located in the United States. Both profit and nonprofit organizations are eligible. Foreign core technological R & D projects, as well as foreign collaborators and subcontractors, are eligible to participate.

2. Contact Information for the NIBIB Scientific Program Staff

For both new applications and competing continuations, prospective grantees are required to discuss the proposed resource grant application and the proposed budget with the NIBIB Scientific Program Staff well in advance of the application deadline. These discussions provide applicants with a clearer understanding of current P41 Center policies, priorities, and any newly instituted guidelines and special situations, such as the inclusion of consortia, subcontracts, etc. Applications that do not meet the P41 Center guidelines will be returned without review.

For all applications that request over $500,000 in annual direct costs, applicants must contact Program Staff at least six weeks prior to the planned submission date to obtain approval to submit an application. Applications with annual direct costs over $500,000 that are received without prior staff approval will be returned without review.

The NIBIB encourages your inquiries and welcomes the opportunity to answer questions from potential applicants. NIBIB scientific program staff and their scientific program areas can be found at http://www.nibib.nih.gov/Research/ProgramAreas. Alternatively you may direct your P41 specific questions to the following two NIBIB scientific staff:

Dr. Christine A. Kelley
Director
Division of Discovery Science and Technology
National Institute for Biomedical Imaging and Bioengineering
6707 Democracy Boulevard, Suite 200
Bethesda, MD 20892
(301) 451-4778
kelleyc@mail.nih.gov

Dr. Alan McLaughlin
Program Director
Division of Applied Science and Technology
National Institute for Biomedical Imaging and Bioengineering
6707 Democracy Boulevard, Suite 200
Bethesda, MD 20892
(301) 496-9321
mclaugal@mail.nih.gov

Studies using vertebrate animals or human subjects in core, collaborative, or service projects require assurances and review by the Institutional Animal Care and Use Committee (IACUC) or Institutional Review Board (IRB), respectively, and must be in compliance with Public Health Service (PHS) policy (for animal welfare) and HHS regulations (for human subjects). This

includes studies involving volunteers. Other assurances may be required, as discussed in the instructions for Form PHS 398.

3. Application Form and Specific P41 Application Instructions

The current version of Form PHS 398, Application for Research Grant, should be used for resource grant applications. Application kits can be found at http://grants2.nih.gov/grants/funding/phs398/phs398.html.

Required information, in addition to that requested in the Form PHS 398 instructions, is listed below by section. Neither a site visit nor an applicant interview is guaranteed as part of the review of the resource grant application. The written application should be complete and stand on its own.

Budget Section (Pages 4-5 of PHS 398 Form): The budget should be completed as described in the instruction sheet for Application for a Public Health Service Grant (Form PHS 398). Funds may be requested for technological R&D, training, dissemination, Scientific Advisory Board meetings (in the consultant costs) and the Resource's expenses associated with collaborative and service projects. Graduate student and postdoctoral support can be requested only if they are active participants in a core research project. The level of the requested budget should be clearly supported by the research plan. The outside investigators of collaborative and service projects must derive support for their projects from sources outside the P41 Center.

The budget justification beginning on PHS Form Page 5 should include a detailed justification for key personnel. The NIBIB requires the PI to devote at least 25% effort to the Center. The percentage effort for all personnel should be specified for a) each of the core projects, b) the collaborative projects, c) service, d) training, and e) dissemination in the budget justification.

A detailed justification should also be supplied for the equipment requested, as well as its maintenance, for the Resource. Appropriate price quotes should be included for major items of equipment and maintenance costing more than $25,000. An evaluation of alternative instruments or manufacturers should be included along with a discussion of the proposed procurement plan. Similar justifications should be provided for any subcontractual or consortium arrangements. Use continuation pages as needed.

A budget ceiling of $700,000 per year in direct cost, excluding equipment cost, and a budget ceiling of $500,000 in equipment for the duration of the requested project are placed on P41 Grants. Only under rare circumstances will applications with budgets exceeding $700,000 be considered. In those cases, strong scientific reasons must be provided in the application and applicants must obtain a written waiver from the NIBIB to exceed the budget ceiling and include it with the submission of their application. The waiver must be requested well in advance of submission of the application. Major equipment purchases (more than $500,000 over the course of the project period) often require support from other sources when the NIBIB is unable to fund the entire request. Plans for such shared funding should be detailed in the application. Applications exceeding these ceilings ($700,000 in direct costs per budget period and/or $500,000 total in equipment for the duration of the requested award) will be returned without review if approval from the NIBIB has not been granted prior to submission.
In accordance with NIBIB policy, recurring direct costs (direct costs excluding equipment) requested for the first year of a competitive renewal application cannot exceed the final non-

competing year's direct recurring costs budget by more than 10%, or the budget ceiling of $700,000, whichever is less. Where this policy may significantly limit the Program scope of the proposed research, the applicant may request a waiver of the 10% ceiling. A letter, clearly justifying the request for a waiver, must be submitted, via the program director, to the NIBIB well in advance of the application receipt date. The waiver to the ceiling must be approved in writing by the NIBIB before the Center's competing renewal application is submitted and accepted.

Biographical Sketch Section: Include standard NIH biographical sketches for all key personnel for whom salary support is requested in the application, and for each of the principal collaborators.

Research Plan Sections A-D: Follow the general PHS 398 instruction. In addition, the following specific instructions are given for a P41 application:

The page limitation specified in the PHS 398 for items A-D of the Research Plan does not apply. The length of sections A-D should be consistent with the scope of the proposed research and the number of collaborative and service projects, but cannot exceed 90 pages. It is important to be concise, but there should be sufficient information about each core, collaborative, and service project to permit its evaluation.

Research Plan C: Preliminary Studies/Progress Report should include a plan that states long-term goals and overall objectives for the Center and a projected timetable for technology development. Information on factors and events contributing to the decision to create the resource and on comparable resources elsewhere should be presented. Applicants should explain in detail what makes this particular resource "unique" in terms of its intellectual and technological capabilities. For competing continuation or supplemental applications, a brief summary of the P41 Center's progress should be included. Include copies of the P41 Center's most recent annual progress report and minutes of the most recent Scientific Advisory Board meeting in the Appendix.

Research Plan D: Research Design and Methods should include a discussion of the proposed research in each of the three major Center activities: technological R&D, collaborative research, and service. Indicate the relative emphasis to be given to these activities and explain the proposed division of effort. Plans for training and dissemination should also be presented.

The following five areas should be addressed:

> ***Technological Research and Development:*** The technological R&D Core projects to be conducted must be presented in detail. For each project describe the background, objectives, rationale, methods and procedures, significance, and facilities available to conduct the project. It is anticipated that some, but not all, of the Core projects may involve exploratory high risk/high impact research. Applicants must clearly define the tool or set of tools being developed in the Core projects and how these tools will impact the collaborative projects. For competing continuation applications, new activities should be specifically identified. If research activities involve support at more than one location through a consortium/contractual arrangement, the application should provide a separate description, detailed budget and budget justification for the consortium/contractual component(s).

The continued development of innovative technology and the steady infusion of new areas of technological R&D are important considerations in reviewing competing continuation proposals. Long-term support depends strongly on the Resource's commitment to the introduction and application of new technology and serving biomedical investigators from an array of institutions on a regional or national basis.

Collaborative Research: Collaborative projects enable non-core researchers to interact with the Resource staff to pursue areas of common interest that further the Resource's research objectives. These projects are selected for the impact they will make on the technological field as well as for advancing the frontiers of biology and medicine.

For each collaborative project, describe the specific objectives: the rationale for the proposed approach to the problem, methods, and procedures to be used; the significance of the proposed work; and the impact of the expertise of the Center's core staff along with the technology developed at the Center on the collaborative project. Provide literature citations. The collaborator's name, institution and funding status of the project including principal investigator, grant number, and project period dates, and also the source of funds should accompany the description of the project. Collaborative projects that have already been peer-reviewed will be evaluated on how they clearly advance and stimulate technological resource development as well as advance the frontiers of biomedical science. Those that have not been peer-reviewed should include more detail and will be evaluated for scientific merit of the research proposed. New applications should have at least four relevant collaborative projects, three of which are with investigators outside the P41 Center's host institution. In competing renewals, the number of collaborative projects is expected to increase significantly, with the majority being from outside the host research institution.

Service: Comprehensive plans for service should be presented. A representative sample of (no more than 20) research projects to be served by the resource should be included. Each project should be described in sufficient detail to allow the reviewers to evaluate the need for the resource technology in the proposed project. The user's name and institution and funding status of the project (including principal investigator, grant number, funding source, and term) should accompany the description of the project. In competing renewals, the P41 Center should strive to provide the major portion of its service to the outside research community. If a charge-back system that results in program income is planned, a description of how costs are to be shared by the users should be included. Additionally, special administrative requirements that apply to program income must be observed. Program income means gross income earned by the recipient that is directly generated by a supported activity or earned as a result of the award (additional information is available in 45 CSR 74.2 and 74.24, which can be obtained by searching the Code of Federal Regulations at http://www.access.gpo.gov/nara/cfr/cfr-table-search.html). An estimate of the amount and source of program income expected to be generated as a result of the P41 Center award must be included on the "Checklist Page" of all competing and non-competing continuation applications. Net program income earned during a budget period must be reported on the long-form Financial Status Report (except for program income earned as a result of inventions, to which special rules apply). Cost incident to the generation of program income may be deducted from gross income to determine program income, provided these costs have not been charged to the award. Program income earned during the project period shall be retained by the P41 Center award recipient and, in accordance with the terms and conditions of the award.

All publications that result from utilization of the P41 Center Grant must acknowledge NIBIB support.

Training: Comprehensive plans for training activities should be presented. Examples of appropriate training activities include: special training on Center facilities for collaborators and service users of the Center on an individual basis; routine training and education on the technology/methodology through hands-on laboratory experience, seminars and lectures on a regular basis; short courses, symposia and workshops on appropriate topics that bring together researchers in multidisciplinary areas from academic institutions, hospitals and industry for discussions on the use of the resource's technology in biomedical research.

Funds to support courses given for credit may not be requested. Individuals involved in the training experiences may not be paid a stipend nor may the training experience be a requirement for receipt of an academic degree.

Dissemination: Comprehensive plans for dissemination of the Center's technology, expertise or accomplishments must be presented. Appropriate dissemination activities involve informing the scientific community about the Center's technology or accomplishments by: publishing articles, books, patents, newsletters, annual reports, special issues of technical journals; web pages; press releases; presenting research results at meetings; conducting conferences; distributing software products; and transferring technologies to industry where they will be distributed widely.
In Centers that are developing software, emphasis should be placed on producing portable, well-documented, user-friendly software, making it readily available to the user community and providing user support.

All dissemination activities must acknowledge NIBIB support.

4. Administrative, Management, and Fiscal Aspects

A separate section on the P41 Center organizational structure should address the following:

Organizational Structure: Describe the organizational structure of the Resource. Indicate how the Resource will relate to the administrative structure of the grantee institution.

Resource Staff Responsibilities: Describe how the principal investigator and the proposed resource staff will be organized with respect to the resource activities: technological R&D, collaborative research, provision of service, training, dissemination and general resource administration. Describe the scientific and technical expertise of the staff that will operate, maintain, and develop the Resource capabilities.

Resource Operating Procedure: Describe operating procedures and policies planned for the Resource. Include criteria and mechanisms to review applications for the use of the resource and for scheduling. Also describe methods for selecting collaborative research and service projects. Include samples of the form to be filled out by the collaborators and users and the instructions on how they are to acknowledge support provided by the Resource in any resulting publications.

Support of Service and Collaborative Projects: Direct support from resource funds for collaborative or user activities are not allowed. For competing continuation applications, when applicable, present a plan for sharing costs for routine service and long-term collaborative projects with funds from outside the resource grant. For resources with a substantial amount of service anticipated, describe fee-for-services. Include instructions on how users are to acknowledge support provided by the Resource in any resulting publications.

Scientific Advisory Board (SAB): Describe the role of the SAB. For example, explain the board's role in advising on instrument purchases, reviewing collaborative and service projects for merit and appropriateness, and allocating resources. The scientific disciplines to be represented by the advisory board should be provided. If already appointed, names of board members and a brief description of their qualifications should also be included. An executive committee, perhaps a local subcommittee of the SAB, may be included as an adjunct to the full SAB as well as a medical committee if there is substantial involvement of human subjects in research projects. Funds may be requested in the consultant category of the budget to support the costs related to the SAB.

5. Deadlines for Submission

The deadlines for submission are February 1, June 1, and October 1

GUIDELINES FOR REVIEW OF NIBIB P41 BIOMEDICAL TECHNOLOGY RESOURCE CENTER APPLICATIONS

A. Review Philosophy

The NIBIB supports P41 Resource Center Grants research in a variety of areas of biomedical science. Applications for such centers are made *via* the P41 funding mechanism, and are reviewed by the Center for Scientific Review (CSR). A resource is centered on technological development, and various aspects of the project must support and make use of the technology. The following information should guide review of a research resource application. P41-supported research resources serve a unique purpose in the broad context of NIH-funded research. This specialized role requires a distinct set of qualities that can be defined largely in terms of their resulting impact on the biomedical sciences. It is the breadth and depth of this impact that are the measure of these resources. It is important that reviewers be mindful of both this overarching mission and the unique qualities that support it. Research resources may be developed in a specific, narrow technological area, or they may represent an integrated approach to the development of tools and methods across a broader line of inquiry. In either case, they represent a critical mass of both technological and intellectual resources assembled with the intent of exploiting advances in instrumentation and methodology for biomedical research. These resources create critical, often unique technology and methods at the forefront of their respective fields that are applicable to a wide variety of problems in the biological sciences. This is accomplished through a synergistic interaction of technical and biological expertise, both within the resources and through intensive collaborations with other leading laboratories. At their best, these resources should be in an optimal position to: identify unexpected opportunities for technological advances to open new lines of biological inquiry, or to apply biological concepts to address engineering problems; and appreciate which problems they may be in a position to solve by creation of new tools. This intense synergy between technology development and the

biological sciences gives the resources a fundamentally different character from that of labs engaged in investigator-initiated or other center-related projects with more narrowly defined goals.

A properly constituted research resource constantly strives to provide service and training to outside investigators and to disseminate the technology and methods it has developed. These efforts require the commitment of far greater financial and personnel resources to non-science activities than might be expected in any other setting. Providing other investigators with ready access to resource tools and personnel has a substantial impact on administration and daily operation of the laboratory. Efforts to train the broader scientific community and disseminate technology require a fundamentally outwardlooking philosophy that may, on the surface, appear at odds with the competitive nature of modern science. The goal of these efforts is to, so far as is possible, export the technology and expertise of the resource into the broader community, achieving a broader impact on biomedical research than would be possible through the projects in which the resource can participate directly. Ultimately, this process should drive toward the widespread and routine application of the technologies being actively disseminated.

B. P41 Resource Center Plan

The 5 required components (technological research and development, collaborative research, service, training, and dissemination) should be clearly described. Absence of sufficient detail in the written proposal on one or more of these will be detrimental in review of the project (and, in fact, may well provide a sufficient basis for the application to be returned without review). Research and development is the major resource activity. Research projects can be divided into two categories: Core (technological research and development) and collaborative. A minimum of three technological R&D projects constitute the Core section of the P41 Center grant. New applications should have at least four relevant collaborative projects, three of which are with investigators outside the P41 Center's host institution. In competing renewals, the number of collaborative projects is expected to increase significantly, with the majority being from the outside the host research institution. Both categories of research are required. The emphasis placed on each research category depends on the goals of the resource and the stage of development of the resource technology and should reflect a balance in terms of the advanced technological needs of the scientific community. While service is one of the key elements of the resource, the P41 mechanism was not designed to support service-only centers. New applicants are expected to have active research and development core and collaborative research projects at the time of application and to detail their plans for expanding these and adding the service, training, and dissemination components, if not yet established. Investigators submitting continuing competing applications are expected to have all five components in place at the time of application.

1. Technological Research and Development

The reviewers should evaluate whether the resource technology is dynamically evolving, state-of-the-art, an important area for research and development in its own right, and likely to advance the frontiers of biomedical research. The resource technology should not be broadly available by other means. An element of high risk (and potentially high payoff) may be present in one or more of the core projects and is appropriate for this component. Investigators should, however, present alternative approaches to solving technological problems in the event that their main conceptual thrust should prove unfeasible. Reviewers should characterize the uniqueness of the

Center's technological goals and the synergy between core and collaborative projects in advancing the focal technology. Reviewers should identify what makes this resource "unique" in the technological goals it is pursuing as well as in the cluster of collaborative projects to which the advanced technology is being applied. In competing continuation requests, reviewers should look for evidence of new meritorious efforts and significant progress during the past grant period.

2. Collaborative Research

The reviewers should determine whether the resource staff is continuously developing new, significant applications of the resource technology in the biomedical sciences through high quality collaborative research projects. The projects served by the new technology should be broad in scope and involve a variety of biomedical research areas.

The resource is expected to be highly responsive to a regional or national user community whose members are funded from other sources such as other NIH or federal agency grants, grants from private organizations, and industry. It is the applicant's responsibility to identify user communities that both need and will use the research capabilities to be provided by the resource. Collaborative projects that have already been peer-reviewed should be evaluated on the basis of how they clearly advance and motivate further technological research and development and for the appropriate use and impact of the new technology on the collaborative project itself. Those that have not been peer-reviewed should include more detail and will be evaluated on the scientific merit of the research proposed; however, it is expected that the majority of collaborative projects are independently funded. As indicated below, resource funds cannot be used directly to support collaborative projects; for example, salaries of personnel working on collaborative projects cannot be part of the resource budget (although it is expected that some funds may support collaborative research efforts at the P41 site). In competing continuing requests, reviewers should evaluate the balance that has developed between collaboration and technology research and development and between collaboration and service. Reviewers should assess whether collaborative projects are driving core research and whether collaborative projects are making good use of the new technological advances. Long term collaborations may roll over into service projects and new collaborators in important biomedical fields should be actively sought to invigorate the resource.

3. Service

Reviewers should determine if the resource is available to outside users. The equipment and technology utilized for service should be state-of-the-art and should meet significant biomedical research needs. The nature of the service projects should be multicategorical and have a regional or national geographical distribution. For resources that do a substantial amount of service, reviewers should evaluate how costs are shared by the users, including fee for service systems.

4. Training

Reviewers should evaluate, in new applications, the adequacy of plans for providing opportunities for training; and, in competing continuation applications, if there have been reasonable results accruing from these efforts to date. Examples of appropriate training activities include the individual, special training given to collaborators and service users; training and education on the technology/methodology through hands-on laboratory experience, on-line

tutorials, seminars and lectures on a regular basis; and short courses, symposia and workshops on the use of the resource's technology in biomedical research.

Training courses offered by the resource may not constitute a requirement for receipt of an academic degree.

5. Dissemination

The reviewers should evaluate in new applications, the adequacy and appropriateness of the proposed plans; and in competing continuation applications, if there has been reasonable and timely progress in this area. Appropriate dissemination activities involve informing the scientific community about the resource's technology or accomplishments by publishing articles, books, patents, newsletters, annual reports, special issues of technical journals, world wide web pages, and press releases; presenting research results at meetings; conducting conferences; distributing software products; and transferring technologies to industry where they will be distributed widely. In resources that are developing software, reviewers should determine if the software is portable when appropriate, well-documented, user-friendly, and readily available to the user community.

Dissemination includes a requirement for outreach to non-expert communities as well as the expert community, to make them aware of the new technology.

C. Administrative, Management, and Fiscal Aspects

The reviewers should evaluate the administrative and managerial aspects presented in the written proposal. In addition, if a site visit takes place, reviewers should examine the discrete space set aside for the resource and the laboratory facilities, including those available to visiting scientists. In the case of a competing continuing application, the log books recording the hours of usage of the instruments and their idle and down time should be examined. Reviewers should take note of which instruments are in place and operational and which staff members are currently on site.

1. Institutional Commitment

Reviewers should evaluate the institution's commitment to the resource. For example, examine allocated space, costs associated with alterations and renovations and purchase of instrumentation and computers, and salary support for some resource staff.

2. Staff Credentials

The reviewers should evaluate the scientific and managerial credentials of the principal investigator and the credentials of other key professional and technical staff.

3. Scientific Advisory Board

Reviewers should evaluate the role of the scientific advisory board, or (in proposed resources) plans for the board (and associated committees such as local executive and medical committees), and whether the members have or will have sufficient breadth and ability to take an effective role in the review and guidance of the resource operations.

4. Scoring

For resource grant applications, each core project in the Technological R&D section should be scored separately. Also, each of the other components of the center, Collaborative Research, Service, Training, and Dissemination should be scored separately. Finally an overall score for the resource grant application should be assigned as shown below. The median score for NIH applications should be about 3.0.

Score
Technological Research and Development
Core Project 1 _____
Core Project 2 _____
Core Project 3 _____
Collaborative Research _____
Service _____
Training _____
Dissemination _____

Overall Score for the Resource _____

The overall score for the resource is generally not the average of the individual scores but rather should take into account the synergy of the individual components and reflect the individual scores weighted in a balance that is appropriate for the goals of the resource and the stage of development of the resource technology. It should also take into consideration the administrative and management aspects of the resource.

For competitive renewals, the overall score should also reflect an evaluation of the accomplishments and progress of the center during the previous grant period.

5. Budget

Details of the budget including the length of the grant period should be discussed after the resource application has been finally scored. Percent effort for personnel should be evaluated in the context of their specific contribution to the research of the resource. Graduate student and postdoctoral support can be requested only if they are active participants in a core research project. Requests for individual instruments or for aggregates of instruments should be consistent with the technological goals of the resource and with the projected timetable for technology development as presented in the application. Activities for which funds may be requested are technological research and development, training, dissemination, advisory committee meetings, and the resource's share of efforts associated with collaborative and service projects. In collaborative and service projects, the outside investigators must derive their primary support from sources outside the resource grant. Individuals not included in the resource budget who

participate in the training experiences may not be paid a stipend. Specific justifications should be given for equipment requests and for any proposed sub-contractual or consortium arrangements. In applications where total annual direct costs excluding equipment exceed any budget ceiling, scientific reasons for exceeding the ceiling must be provided in the application. Major equipment requests should include a plan for obtaining funding from other sources should the funding institute be unable to support the full request for equipment. All budget requests that exceed the ceiling for direct costs, excluding equipment, and/or $500,000 for equipment for the full duration of the grant application must receive a written waiver from the program director. The direct recurring costs (excluding equipment) requested for the first year of a competitive renewal application cannot exceed the last year's direct recurring costs budget by more than 10%.

D. Human Subjects and Vertebrate Animals

Any additional data reviewers request for clarification should be obtained and distributed before the review. The IRB and IACUC review may be delayed until funding has been approved, but must be completed and approvals submitted to the funding institute before an award can be made. The institution applying for the resource is responsible for obtaining overall IRB and IACUC approvals, regardless of whether collaborative projects have separate approvals, perhaps at another institution.

1. Protection of Human Subjects from Research Risks

Evaluate the application with reference to the following criteria: risk to subjects, adequacy of protection against risks, potential benefit to the subjects and to others, and importance of the knowledge to be gained. (If the applicant fails to address all of these elements, notify the SRA immediately to determine if the application should be withdrawn.) If all of the criteria are adequately addressed, and there are no concerns, write "Acceptable Risks and/or Adequate Protections." A brief explanation is advisable. If one or more criteria are inadequately addressed, write, "Unacceptable Risks and/or Inadequate Protections" and document the actual or potential issues that create the human subjects concern. If the application indicates that the proposed human subjects research is exempt from coverage by the regulations, determine if adequate justification is provided. If the claimed exemption is not justified, indicate "Unacceptable" and explain why you reached this conclusion. Also, if a clinical trial is proposed, evaluate the Data and Safety Monitoring Plan. (If the plan is absent, notify the SRA immediately to determine if the application should be withdrawn). Indicate if the plan is "Acceptable" or "Unacceptable", and, if unacceptable, explain why it is unacceptable.

2. Gender, Minority and Children Subjects

Public Law 103-43 requires that women and minorities must be included in all NIH-supported clinical research projects involving human subjects unless a clear and compelling rationale establishes that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. NIH requires that children (individuals under the age of 21) of all ages be involved in all human subjects research supported by the NIH unless there are scientific or ethical reasons for excluding them. Each project involving human subjects must be assigned a code using the categories "1" to "5" below. Category 5 for minority representation in the project means that only foreign subjects are in the study population (no U.S. subjects). If the study uses both then use codes 1 thru 4.

1 Both Genders, Minority & Non-Minority, Children & Adults
2 Only Women, Only Minority, Only Children
3 Only Men, Only Non-Minority, No Children Included
4 Gender Unknown, Minority Representation Unknown, Representation of Children Unknown
5 Only Foreign Subjects

Examine whether the minority and gender characteristics of the sample are scientifically acceptable, consistent with the aims of the project, and compliant with NIH policy. For each category, determine if the proposed subject recruitment targets are "A" (acceptable) or "U" (unacceptable). If you rate the sample as "U", consider this feature a weakness in the research design and reflect it in the overall score. Explain the reasons for the recommended codes; this is particularly critical for any item coded "U".

NOTE: To the degree that acceptability or unacceptability affects the investigator's approach to the proposed research, such comments should appear under "Approach" in the five major review criteria above, and should be factored into the score as appropriate.

3. Vertebrate Animals

Express any comments or concerns about the appropriateness of the responses to the five required points (*See* instructions to NIH application Form 398); especially whether the procedures will be limited to those that are unavoidable for the conduct of scientifically sound research.

4. Biohazards

Note any materials or procedures that are potentially hazardous to research personnel and indicate whether the protection proposed will be adequate.